The Examiner objected to the limitation "20-10000" in claim 23 as being new matter. Claim 23 has been amended to recite "100-10000", as recited in originally filed claim 1. The amendment was made solely to overcome the objection and not for the purpose of distinguishing the invention from the cited art. Withdrawal of the objection is requested.

Claims 20-23 were rejected under 35 USC § 103 as being obvious over Callahan et al., Finkenaur, Reissman et al. and Moore, taken with Sauerbier et al. This rejection is traversed for the following reasons.

The present application claims pharmaceutical preparations. Applicants submit that a person of ordinary skill in the art of preparing such formulations would not incorporate or combine the cited references. In particular, the teaching of Callahan et al., of solubilization of a heptapeptide in acetic acid would not have been considered, since the methods described By Callahan are employed in the manufacturing and purification of crude peptides, and not in the preparation of pharmaceuticals for human use.

In the attached publication on peptide formulations (Niu and Chui, Journal of Pharmaceutical Sciences, vol. 87, No. 11, pp. 1331-1334, November, 1998) it is stated at page 1333 that for liquid formulations the major degradation pathways are hydrolysis deamidation and isomerization. It is also stated that in the case of lyophilized powder, the degradation

patterns are similar to those observed in solution. Since it is known to skilled artisans that hydrolysis and deamidation are reactions that are also caused by acids, it is submitted that the use of acetic acid as a stabilizer produces a result which would be unexpected to a person of ordinary skill in the art of preparing pharmaceutical formulations for human use.

It is submitted further submitted that the Sauerbier reference also provides no suggestion or motivation toward the claimed invention because it only teaches sterile filtration and lyophilization of ifosfamide, not to any peptide. A person of skill in the art would not have been motivated to combine this reference with any of the other cited references.

Applicants submit that it is not correct to generalize the methods for sterile filtration and lyophilization independently of composition for substances to be used in pharmaceutical form. As indicated in the Niu and Chiu reference, on page 1331, it is important that the physical properties of each peptide be taken into account during such purification.

Callahan (US 4,908,475) teaches solubilization of a linear peptide in approximately 100-10,000 parts by weight of acetic acid followed by lyophilization. Then the crude peptide was purified by gel filtration in order to obtain the purified, linear peptide. Callahan does not describe pharmaceutical process to produce a sterile lyophilisate of an

LH-RH antagonist for medical use, but rather the isolation and purification of heptapeptides which are different from cetrorelix and which do not exhibit the problem of gel formation. Thus, the Callahan reference would not lead a person of skill in the art to the present invention.

The Finkenauer patent discloses a stable composition comprising a polypeptide growth factor and a water soluble, swellable, pharmaceutically acceptable polymer capable of imparting viscosity to a reconstituted solution of the composition. The presence of the bulking agent mannitol is only named in connection with a composition containing a gel forming preparation. It is respectfully submitted that a decapeptide such as Cetrorelix cannot be compared with a polypeptide, the physicochemical properties being very different. A person of skill in the art would not be motivated to combine Finkenauer with the other cited references to yield the present invention.

Reissmann shows in a scientific, pharmacological article the effect of Cetrorelix acetate or trifluoroacetate on DMBA induced mammary carcinoma. A medically usable, sterile, lyophilized Cetrorelix is not described.

Thus, none of these references, nor any combination thereof, would lead a person of skill in the art to the sterile lyophilisate of a peptide.

For all of the above reasons, it is submitted that the

presently claimed invention is not obvious from the cited references, either alone, or in combination. Withdrawal of the 35 USC § 103 rejection is respectfully requested.

All rejections having been addressed, it is respectfully submitted that this application is in condition for allowance, and Notice to that effect is respectfully requested.

Respectfully submitted,

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